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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/708,974	11/08/2000	Philip A. Beachy	JHUC-P03-010	3945

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EXAMINER

BADIO, BARBARA P

ART UNIT PAPER NUMBER

1616

DATE MAILED: 11/28/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/708,974

Applicant(s)

BEACHY ET AL.

Examiner

Barbara P Badio, Ph.D.

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☐ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 2,4,9,10 and 24-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1,3,5-8 and 18-20 is/are rejected.
- 7) ☐ Claim(s) 11-17 and 21-23 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_.
- ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

**First Office Action on the Merits**

***Election/Restrictions***

1. Applicant's election with traverse of Group I and the species of cycloamine, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that Groups I, III and V could be examined simultaneously without significant additional burden to the examiner and that the elected species is not representative of all compounds encompassed by Formula I. This is not found persuasive because a search of the entire scope of the invention would present a significant and serious burden on the examiner due to the scope of the claimed compounds. It would require several different search strategies and a reference against one Group might be applicable to the others. However, if applicant feels the different species are not patentably distinct, as stated in the previous Office Action, applicant should make it of record (see paragraph 7 of the previous Office Action).

The requirement is still deemed proper and is therefore made **FINAL**.

2. Based on applicant's election, claims 2, 4, 9, 10 and 24-26 stand withdrawn from further consideration as being drawn to a nonelected invention. Claims 1, 3, 5-8 and 11-23 will be examined to the extent they read on the elected species, cycloamine, and obvious variants thereof.

### ***Claim Objections***

3. Claims 11-17 and 21-23 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 11-17 and 21-23 are not been further treated on the merits.

### ***Double Patenting***

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1, 3, 5-8 and 18-20 are provisionally rejected under the judicially created doctrine of double patenting over claims 3, 5-8, 11-17, 20, 30, 31, 43 and 44 of copending Application No. 09/090,622. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application

and the instant application are claiming common subject matter, as follows: a method for inhibiting paracrine and/or autocrine signals using steroidal alkaloid.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

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6. Claims 1, 3, 5-8 and 18-20 are rejected under the judicially created doctrine of double patenting over claims 1 and 2 of U. S. Patent No. 6,288,048 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: they are both drawn to a method of inhibiting a paracrine and/or autocrine signal by administration of a hedgehog antagonist.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application, which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1 and 18-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds found in figure 1, does not reasonably provide enablement for all hedgehog antagonists. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims are drawn to the use of any hedgehog antagonist (known and unknown) for the inhibition of all paracrine and/or autocrine signals. The present specification lacks guidance as to how one having ordinary skill in the art would make and use compounds commensurate in scope with the instant claims.

9. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 3 recites the phrase "wherein, as valence and stability permit". The present specification lacks guidance as to how the ordinary artisan in the art would readily determine the stability of the compounds without undue experimentation.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 3, 5-8 and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 5 recite "e.g." and "preferably", respectively, which render the claims indefinite because it is unclear whether the limitations that follow are part of the claimed invention.

Claims 5-8 lack definition of the various R groups identified by the instant claims. It is noted that the claims recite the groups are as defined above. If by "defined above" applicant means a previous claim, it is suggested that said phrase be rewritten as "defined in claim #".

Claim 6 recites "T and T' taken together with the ring A or B form a covalently closed ring of 5-8 ring atoms". T and T' are not identified on the same structure as A and, thus, it is unclear how T and T' will form a ring with A. Does applicant intend the combination of the two structures?

### ***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

13. Claims 1, 3, 5-8 and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerashchenko et al.

Gerashchenko et al. teach the compound jervine and its anti-inflammatory activity (see the attached Abstract). The method of use of the compound taught by the reference is encompassed by the instant claims.

14. Claims 1, 3, 5-8 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Beachy et al. ('091).

Beachy et al. teach the compound jervine and its inhibition of cholesterol biosynthesis (col. 11, lines 8-9; col. 75, lines 36-45). The method of use of the compound taught by the reference is encompassed by the instant claims.

15. Claims 1, 3, 5-8 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Beachy et al. ('048).

Beachy et al. teach the compound jervine and cyclopamine and their inhibition of cholesterol biosynthesis (Abstract; Fig. 6; col. 3, lines 18-29; col. 20, claims 1 and 2). The method of use of the compound taught by the reference is encompassed by the instant claims.



***Claim Rejections - 35 USC § 103***

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gerashchenko et al.

Gerashchenko et al. teach the compound jervine and its anti-inflammatory activity (see the attached Abstract).

Claim 18 differ from the reference by reciting the in vitro contacting of cells with the claimed compound. However, the use of in vitro model in determining the activity of any compound, including those of the instant claim, involves routine experimentation utilizing any of the known in vitro tests, including those used in the testing of the inflammatory property of a compound. The motivation to do in vitro testing is to determine the optimum concentration at which the compound is effective.

18. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beachy et al. ('091).

Beachy et al. teach the compound jervine and its inhibition of cholesterol biosynthesis (col. 11, lines 8-9; col. 75, lines 36-45).

Claim 19 differs from the reference by reciting the in vivo contacting of cells with the claimed compound. However, it is routine in the art to determine the efficacy of a useful compound in vivo. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to administer the prior art compound in vivo in order to determine the efficacy of said compound. The ordinary artisan would expect the compound to have similar in vivo activity and, thus, he would have the reasonable expectation that the prior art compound would inhibit cholesterol biosynthesis in vivo. Therefore, the claimed invention is prima facie obvious.

19. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beachy et al. ('048).

Beachy et al. teach the compound jervine and cyclopamine and their inhibition of cholesterol biosynthesis (Abstract; Fig. 6; col. 3, lines 18-29; col. 20, claims 1 and 2).

Claim 19 differs from the reference by reciting the in vivo contacting of cells with the claimed compound. However, it is routine in the art to determine the efficacy of a useful compound in vivo. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to administer the prior art compound in vivo in order to determine the efficacy of said compound. The ordinary artisan would expect the compound to have similar in vivo activity and, thus, he would have the reasonable expectation that the prior

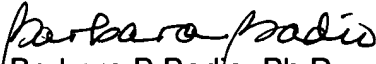
art compound would inhibit cholesterol biosynthesis in vivo. Therefore, the claimed invention is prima facie obvious.

***Telephone Inquiry***

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P Badio, Ph.D. whose telephone number is 703-308-4595. The examiner can normally be reached on M-F from 7:30am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

  
Barbara P Badio, Ph.D.  
Primary Examiner  
Art Unit 1616

BB  
November 27, 2001